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## ACCEPTED MANUSCRIPT

# Maternal nicotine exposure has severe cross-generational effects on offspring behavior

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#### **Highlights:**

- Maternal pre-pregnancy nicotine exposure could also lead to depression-like behaviors in the offspring rather than have to through the uterine environment.
- Biparental pre-pregnancy nicotine exposure mainly caused a depressive phenotype among F1 mice, and a few with hyperactivity.
- The impact of maternal nicotine exposure on the behavior of the offspring was far severer than that of paternal exposure.
- These effects appear to be mediated via disruption of the balance between GSK3 and p-GKS3 by nicotine.

#### Abstract:

Our previous studies showed that paternal nicotine exposure can lead to hyperactivity in the offspring. Nevertheless, the cross-generational effects of maternal and biparental nicotine exposure remain unclear. In this study, female and male mice were exposed respectively by

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